Remarks

Claims 1-8 and 11 were pending. By this amendment, claims 2, 4-5, and 7-8 are cancelled without prejudice, and claims 12-15 are added. Therefore, claims 1, 3, 6 and 12-15 are now pending.

Amendments to the claims

Support for the amendments and new claim can be found throughout the specification, for example:

Claim 1: page 8, lines 28-29; page 21, lines 1 to 3; claims 2 and 5.

Claim 6: page 14, line 29 to page 15, line 6; examples on pages 18 to 21; page 21, lines 1 to 3; and claims 7 and 8.

Claim 12: claim 3.

Claims 13-14: page 18, line 10.

Claim 15: page 18, lines 28-29.

No new matter has been added by these amendments.

Amendments to the specification

The abstract of the specification was objected to because the term "TTC" was not spelled-out the first time it appeared in the specification.

The term "TTC" does not appear in the abstract. However, Applicants have amended the abstract to spell-out the term "HGF" which does appear in the abstract.

In addition, the first instance of the term "TCC" on page 17, line 24 is now spelled-out. Although there is no literal support of the formal chemical name of TTC in the specification, as evidenced by Prestigiacomo *et al.* (*Stroke*, 30:1110-1117, 1999, Exhibit A), the chemical name of TTC was known to persons skilled in the art at the time of filing the present application (see page 1111, right column, last paragraph of "Quantitation of Cerebral Infarct Volumes", line 6).

In view of these amendments, Applicants request that the objection to the specification be withdrawn.

Information Disclosure Statement

It is noted on page 2 of the Office action that the article, Ishida *et al.* (*Noshinkei*, 2002, March, Vol.54, No.3, pages 213 to 219) published in Japanese cited on the IDS filed on March 7, 2005 fails to comply with 37 CFR §1.98(a)(2) because no copy of Ishida *et al.* was in the file of record.

Enclosed is a copy of Ishida *et al.*, along with a translation of the parts of Ishida *et al.* relevant to the present application. Therefore, Applicants request that the Examiner now consider this document.

Double patenting

Claims 1-4, 6, 7 and 11 are rejected under the judicially created obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,936,594, which the applicant of the present application commonly owns. Claims 5 and 8 are free of rejection.

Claims 2, 4, 7 and 11 have been canceled. Claims 1 and 6 have been amended by incorporating the language of claims 5 and 8 respectively, which are free of the rejection. Therefore, Applicants request that the non-statutory obviousness-type double patenting rejection be withdrawn.

Claim objections

Claims 4, 5, 8 and 11 are objected to because the abbreviation of "HVJ" is not spelled-out the first time it appears in the claims.

Claims 4, 5, 8 and 11 have been canceled, making the objection moot as to these claims. In addition, claim 1 has been amended by incorporating the language of claim 5, which the "HVJ-envelope" has been defined as "hemagglutinating virus of Japan (HVJ)-envelope." Support can be found on page 11, line 33 of the specification.

In view of these amendments, Applicants request that the objection to the claims be withdrawn.

35 U.S.C. § 101

Claims 1-8 and 11 are rejected under 35 U.S.C. § 101 because the recitation of "a nucleic acid" in claims 1 and 8 is directed to non-statutory subject matter. Applicants request reconsideration.

Claims 1 and 6 have been amended to clarify that the "nucleic acid" is "an isolated nucleic acid." The remaining claims depend from claim 1 or 6. In view of these amendments, Applicants request that the 35 U.S.C. § 101 rejection be withdrawn.

35 U.S.C. § 112, first paragraph, written description

Claims 1-8 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It is alleged that the specification does not describe the complete structure of a representative number of species of the large genus of nucleic acids encoding a protein effective as a hepatocyte growth factor. Applicants disagree and request reconsideration.

The claims as filed indicate that any nucleic acid encoding HGF can be used to practice the present invention. Although the specification only particularly mentions human HGF, those skilled in the art would appreciate that any HGF sequence can be used, as numerous HGF sequences were publicly available at the time of the invention. For example, as shown in the enclosed Exhibits B-E, HGF protein sequences (and their corresponding nucleic acid sequences) were available for several organisms, including human, mouse, cat, and Xenopus prior to the filing of the present application. "A patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01. As a result, the claims should not be limited to human HGF as the claims as filed indicate any HGF sequence can be used, and HGF sequences from many different organisms were known to those skilled in the art at the time of the present invention.

Therefore, Applicants request that the 35 U.S.C. § 112, first paragraph, written description rejection be withdrawn.

35 U.S.C. § 112, first paragraph, enablement

Claims 1-8 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicants disagree and request reconsideration.

The Examiner has acknowledged that the following inventions are enabled (page 8, lines 1 to 9; and page 13, line 19 to page 14, line 4 in the Office Action): "an agent for reducing the infarcted area of a cerebral infarction, wherein said agent comprises a nucleic acid encoding a hepatocyte growth factor protein and; a method for reducing the infarcted area of a cerebral infarction comprising administration of said nucleic acid encoding a hepatocyte growth factor protein by direct injection into the subarachnoid space of a subject, wherein said method results in a reduction of the infarcted area."

In order to expedite prosecution, the claims have been amended to clarify that the agent for reducing the infarcted area of a cerebral infarction comprises a nucleic acid encoding a hepatocyte growth factor protein, and that the a method is a method for reducing the infarcted area of a cerebral infarction, wherein the method includes administration of a nucleic acid encoding a hepatocyte growth factor protein by direct injection into the subarachnoid space of a subject.

In view of these amendments, Applicants request that the 35 U.S.C. § 112, first paragraph, enablement rejection be withdrawn.

35 U.S.C. § 112, second paragraph

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, by alleging that the term of "effective" has not been defined by the specification. Claims 6-8 and 11 have also been rejected because claim 6 does not recite any positive step which clearly relates back to the preamble. Applicants request reconsideration.

Claim 1 has been amended to remove the term "effective".

Claim 6 has been amended to recite a positive step that relates back to the preamble.

In view of these amendments, Applicants request that the 35 U.S.C. § 112, second paragraph rejections be withdrawn.

35 U.S.C. § 102(b) and (e)

Claims 1-4, 6, 7 and 11 are rejected under 35 U.S.C. § 102(b) as being anticipated by Morishita *et al.* (Australian Patent Appl. No. 200073148 B2, now Patent No. 774990), and under 35 U.S.C. § 102(e) as being anticipated by Morishita *et al.* (U.S. Patent No. 6,936,594).

Although Applicants disagree, in order to expedite prosecution, claims 2, 4, 7 and 11 have been canceled, and claims 1 and 6 are amended by incorporating the language of claims 5 and 8 (which were not rejected under 35 U.S.C. § 102). Therefore, with respect to the rejection under 35 U.S.C. §102(e) over Morishita *et al.* (U.S. Patent No. 6,936,594) rather than filing an Affidavit by the representative of the Assignee under 37 C.F.R. §1.130 to show common ownership of Morishita *et al.* with that of the present application, claims 1 and 6 have been amended to be distinct from the inventions described in the Morishita *et al.* patent.

In view of these amendments, Applicants request that the 35 U.S.C. § 102 rejections be withdrawn.

35 U.S.C. § 103(a)

Claims 5 and 8 are rejected under 35 U.S.C. §103(a) as being unpatentable over Morishita *et al.* (Australian Patent Appl. No. 200073148 B2, published on April 24, 2001, now Patent No. 774990) in view of Ramani *et al.* (*Proc. Natl. Acad. Sci., USA,* 95:11886-90, 1998). Applicants disagree and request reconsideration.

Not all limitations present in claims 1 and 6 (which include the language of claims 5 and 8, respectively) are taught or suggested by the documents cited. As acknowledged by the Examiner, Morishita *et al.* do not teach or suggest a nucleic acid encoding HGF in the form of an HVJ-envelope. However, Morishita *et al.* also fail to teach or suggest reduction of an infarcted area by administering to a subject the agent comprising an HGF-encoding nucleic acid and an HVJ-envelope. As acknowledged by the Examiner, Ramani *et al.* are silent about a nucleic acid encoding HGF in the form of an HVJ-envelope. However, Ramani *et al.* also fail to disclose or suggest delivery in vivo or administration of an agent comprising HGF-coding nucleic acids and HVJ-envelope into any cerebral region. Instead, Ramani *et al.* describe the delivery of the CAT gene contained in F-virosomes (genetically engineered HN protein-lacking HVJ-envelope) into liver. Ramani *et al.* are also silent on the reduction of the infarcted area of a cerebral infarction by administering the agent to any cerebral region.

As the references cited neither describe nor suggest all of the claim limitations as required by MPEP 2143.03, the claims of the present application are not prima facie obvious.

In addition, *Ramani et al. teach away from the present invention.* Ramani *et al.* describes the delivery of CAT gene contained in the F-Virosomes which are devoid of HN-protein into mouse liver, lung, kidney and spleen. As Figure 2B of Ramani *et al.* shows, CAT gene expression was detected in mouse liver, whereas no significant CAT gene expression was observed in all the other-tested organs (lung, kidney and spleen). Ramani *et al.* further describes as follows (on page 11887, RESULTS, line 2 to page 11888, left column, lines 9).

> "The CAT gene expression was assessed both at the level of mRNA and of protein. Maximum CAT expression was achieved in the liver at a dose of 2μg of DNA loaded in F-virosomes (Fig. 1). RT-PCR analysis of total RNA from various organs confirmed the presence of CAT-specific transcripts in mouse liver (Fig. 2A). Other organs analyzed, i.e., lung, kidney, and spleen, did not express significant CAT transcripts except a very faint RT-PCR signal in case of lungs. CAT gene expression was not detected in tissues like heart, muscle, brain, lymph nodes, skin, and tail." (emphasis added)

Therefore, the data in Ramani *et al.* show that their HVJ-envelope failed to deliver the gene into any organ or and tissue except for liver. In other words, Ramani *et al.* teaches to those skilled in the art that the HVJ-envelope they used for gene delivery is available for liver only. Accordingly, Ramani *et al.* (even in combination with Morishita *et al.*) teach away from the present invention. Therefore the claims of the present application are not obvious.

There was no reasonable expectation of success and no motivation to arrive at the present invention. As discussed above, neither Morishita *et al.* nor Ramani *et al.* teach or suggest the present invention, and Ramani *et al.* teach away from the present invention. Accordingly, even if the cited documents were considered by one skilled in the art, they would not have been motivated to arrive at the present invention.

Because the prior art cited does not teach or suggest present invention, and even teaches away from the present invention, one skilled in the art would not be motivated to arrive at the present invention. Therefore, Applicants request that the 35 U.S.C. § 103(a) rejections be withdrawn.

If any minor issues remain before a Notice of Allowance is issued, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

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